

REGEEnLIFE

Category:

Best Startup

Company Name:

REGEEnLIFE

Turnover and/or Funding:

Currently, REGEEnLIFE is a clinical-stage medtech company and does not yet generate turnover from product sales, as its therapeutic device is still undergoing validation before market authorization.

On the funding side:

- The company has raised private equity (€ 8.5 M) and seed funding from strategic investors and business angels to support R&D, clinical trials, and regulatory activities.
- has secured around € 3 M in non-dilutive funding from public regional, national innovation programs (e.g., Bpifrance) and banks.

An additional funding round will be completed in the next months to support final clinical phases, regulatory clearance, and commercial scale-up, especially for the European market.

Sub-Category:

Medical Technology / Digital Health

Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):

REGEEnLIFE was founded in 2016 by Guillaume Blivet and other co-founders in Montpellier, south of France. His inspiration came after discovering the therapeutic potential of photomedical applications with dermatologists during a conference. Fascinated by photobiomodulation's anti-inflammatory and regenerative effects, Blivet began investigating its potential for neurological applications, particularly in Alzheimer's disease.

Seeing that photobiomodulation works on a cellular level via the mitochondria, Blivet envisioned applying it to brain health. He built a multidisciplinary team of experts in neuroscience, physics, and engineering, and they designed a dual-target PBM device to

stimulate both the brain and the gut, aiming to leverage the gut-brain axis for enhanced therapeutic effect.

The team overcame significant technical hurdles, developing custom optical systems using lasers and guides to bypass hair and optimize light delivery to the brain, culminating in a non-invasive, ergonomic prototype supported by early French public funding. Preclinical studies in mice showed that targeting both the brain and the gut synergistically improved therapeutic outcomes. These promising results laid the foundation for further clinical development.

Alzheimer's disease and related dementias affects over 55 million people globally, a number expected to double by 2050 due to aging populations. It is a major public health crisis with no definitive cure and only limited symptomatic treatments, mostly pharmacological (e.g., cholinesterase inhibitors, new anti-amyloid antibodies). These treatments often offer modest clinical effects, have cost/accessibility limitations, and may involve significant side effects or require invasive administration (e.g., infusions).

Current treatments have limited efficacy, often come with invasive administration, and fail to halt disease progression.

Neuroinflammation, mitochondrial dysfunction, and systemic factors like the gut-brain axis are increasingly recognized as core drivers of Alzheimer's and other neurodegenerative diseases.

REGENLIFE's solution targets these mechanisms non-invasively, with a photobiomodulation-based medical device, offering a new therapeutic class.

So, regarding patients and their families, there is a critical need for safe and non-invasive therapeutic options that support brain health and neuroprotection.

REGENLIFE's neurotech device is designed to address this need: pain-free, home- or clinic-compatible therapy with targets biological mechanisms not addressed by drugs. There is an excellent patient adherence, ease of use, and compatibility with current care pathways.

History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations):

REGENLIFE was founded in 2016 to address the urgent unmet need in neurodegenerative diseases, particularly Alzheimer's disease, by leveraging a photobiomodulation medical device as a novel, non-invasive therapeutic modality to treat the brain.

REGENLIFE has built a robust patent portfolio around its proprietary photobiomodulation technology, designed specifically for neurological applications. The team engineered a

custom optical setup that integrates both LEDs and lasers across multiple wavelengths in the red and near-infrared spectrum, enabling deeper and more targeted light penetration. Because hair is a significant barrier to light, optical guides have been designed to concentrate the rays and deliver photons directly to the scalp. In 2018, a brain-gut application was evaluated in a preclinical model of Alzheimer's disease, which showed that dual application of REGENLIFE's photobiomodulation on both the brain and the gut had significantly greater therapeutic performance compared to brain-only application. REGENLIFE has developed a medical device in the form of a helmet and an abdominal belt. The company has focused on designing a modular medical device to ensure ergonomic fit for both head and abdomen, extend the product's lifespan, and minimize the need for replacements. The system is software-driven, allowing for the customization of therapeutic protocols.

In 2019, efforts focused on refining the physical design of the technology and enhancing the reproducibility of animal studies. These developments laid the groundwork for a highly safe and technically advanced medical device, compliant with stringent safety regulations and uniquely protected by several patents. Photonic diffusion into the brain has been evaluated through Monte Carlo simulations in partnership with Paris-Saclay University.

REGENLIFE's technology is protected by a strong international IP portfolio, with 33 patents across 4 families. These patents cover this unique tri-photonic stimulation approach with a dual-target design (brain and gut), as well as the device architecture, including ergonomic features and light-guiding technologies.

Preclinical studies on animal models of Alzheimer's disease, depression (collaboration with the University of Barcelona), and multiple sclerosis (in collaboration with CNRS and Aix-Marseille University) have demonstrated improvements in cognitive and motor functions, a reduction in neuroinflammation, activation of cellular repair mechanisms, and a synergistic effect from simultaneous gut and brain stimulation, supporting the relevance of the gut-brain axis approach.

In 2022, a first-in-human clinical trial on Alzheimer's disease was published, showing excellent safety and patient compliance, along with some cognitive improvements after only two months of treatment (where anti-Alzheimer's treatments are typically evaluated over an average period of 18 months). This enabled REGENLIFE to initiate a pivotal randomized clinical trial (NCT05926011) on mild-to-moderate Alzheimer's disease in 2023. Five investigational centers (in partnership with Toulouse University Hospital's G rontop le and AP-HP) are currently enrolling a total of 108 patients. The study is expected to be completed by the end of 2026.

REGENLIFE has also recently completed a pilot trial (in collaboration with the AP-HP) on sport-related concussion (NCT05647304), including 50 athletes suffering from concussion. The results will be published soon, and EU market approval (MDR) is

scheduled for submission in September 2025, ahead of commercialization in Europe.

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:

REGENLIFE's medical device represents a groundbreaking convergence of photobiomodulation, neurotechnology, and systemic therapy, offering a non-invasive, multi-target approach to treating neurological conditions. Unlike conventional treatments that rely on pharmaceuticals targeting single pathways, this device uses electromagnetic emissions to stimulate cellular metabolism and reduce inflammation in both the brain and gut; a novel approach based on the emerging science of the gut-brain axis. It's the first technology-based therapeutic specifically engineered to simultaneously target these two regions using a tri-photonic, dual-site stimulation, embedded in an ergonomic, software-driven medical device.

The technology opens up an entirely new avenue for exploring light-based interventions in complex systemic and neurological diseases, including Alzheimer's, depression, multiple sclerosis, and traumatic brain injury. Its design facilitates repeatable, controlled research, and its non-invasive nature makes it an ideal platform for longitudinal studies and combinatory protocols with other treatments (e.g., cognitive therapies, pharmacological interventions, microbiome-based interventions). Furthermore, it may accelerate scientific understanding of neuroinflammation, cellular bioenergetics, and brain-gut interactions, paving the way for personalized neuromodulation therapies.

REGENLIFE's device offers hope in areas where therapeutic options are scarce, costly, or ineffective, especially for patients with Alzheimer's disease. By improving cognitive function, reducing neuroinflammation, and enhancing quality of life with minimal side effects, it supports healthier aging and better disease management. Its ease of use and high patient compliance mean that it could be deployed not just in hospitals and clinics, but also in home-based care, broadening access. In the long term, it may contribute to reducing the social and economic burden of neurodegenerative diseases globally.

Please provide appropriate references (PubMed, Abstract, Website):

Blivet G, Meunier J, Roman FJ, Touchon J. Neuroprotective effect of a new photobiomodulation technique against A β 25-35 peptide-induced toxicity in mice: Novel hypothesis for therapeutic approach of Alzheimer's disease suggested. *Alzheimers Dement* (N Y). 2018 Feb 2;4:54-63. doi: 10.1016/j.trci.2017.12.003.

Abstract

Introduction: Photobiomodulation was assessed as a novel treatment of Alzheimer's disease (AD) by the use of a new device RGn500 combining photonic and magnetic

emissions in a mouse model of AD.

Methods: Following the injection of amyloid β 25-35 peptide in male Swiss mice, RGN500 was applied once a day for 7 days either on the top of the head or the center of abdomen or both.

Results: RGN500 daily application for 10 min produced a neuroprotective effect on the neurotoxic effects of amyloid β 25-35 peptide injection when this type of photobiomodulation was applied both on the head and on the abdomen. Protection was demonstrated by memory restoration and on the normalization of key markers of AD (amyloid β 1-42, pTau), oxidative stress (lipid peroxidation), apoptosis (Bax/Bcl2) and neuroinflammation.

Discussion: RGN500 displays therapeutic efficacy similar to other pharmacological approaches evaluated in this model of AD.

Keywords: Alzheimer's disease; Amyloid β ; Electromagnetic; LLLT; Magnetic; Memory; Neurodegenerescence; Neuroinflammation; Oxidative stress; Phosphorylated tau; Photobiomodulation; Photonic.

<https://pubmed.ncbi.nlm.nih.gov/29955652/>

<https://alz-journals.onlinelibrary.wiley.com/doi/10.1016/j.trci.2017.12.003>

Blivet G, Relano-Gines A, Wachtel M, Touchon J. A Randomized, Double-Blind, and Sham-Controlled Trial of an Innovative Brain-Gut Photobiomodulation Therapy: Safety and Patient Compliance. *J Alzheimers Dis.* 2022;90(2):811-822. doi: 10.3233/JAD-220467.

Abstract

Background: Recent innovative non-pharmacological interventions and neurostimulation devices have shown potential for application in the treatment of Alzheimer's disease (AD). These include photobiomodulation (PBM) therapy.

Objective: This pilot study assesses the safety, compliance with, and efficacy of a brain-gut PBM therapy for mild-to-moderate AD patients.

Methods: This double-blind, randomized, monocentric sham-controlled study started in 2018 and ended prematurely in 2020 due to the COVID-19 pandemic. Fifty-three mild-to-moderate AD patients were randomized, 27 in the PBM group and 26 in the sham group. All patients had 40 treatment sessions lasting 25 min each over 8 weeks and were followed for 4 weeks afterwards. Compliance with the treatment was recorded. Safety was assessed by recording adverse events (AEs), and efficacy was evaluated using neuropsychological tests.

Results: The PBM therapy proved to be safe in regard to the number of recorded AEs (44% of the patients), which were balanced between the PBM and sham groups. AEs were mainly mild, and no serious AEs were reported. The majority of the patients (92.5%) were highly compliant, which confirms the feasibility of the PBM treatment. Compared to the sham patients, the PBM patients showed lower ADAS-Cog comprehension subscores, higher forward verbal spans, and lower TMT-B execution times, which suggests an improvement in cognitive functions.

Conclusion: This study demonstrates the tolerability of and patient compliance with a PBM-based treatment for mild-to-moderate AD patients. It highlights encouraging efficacy trends and provides insights for the design of the next phase trial in a larger AD patient sample.

Keywords: Alzheimer's disease; brain-gut axis; cognition; dementia; memory; neurodegenerative diseases; optics and photonics; photobiomodulation.

<https://pubmed.ncbi.nlm.nih.gov/36189591/>

https://journals.sagepub.com/doi/10.3233/JAD-220467?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%20pubmed

Durdevic L, Relaño Ginés A, Roueff A, Blivet G, Baffou G. Biomass measurements of single neurites in vitro using optical wavefront microscopy. *Biomed Opt Express*. 2022 Nov 17;13(12):6550-6560. doi: 10.1364/BOE.471284.

Abstract

Quantitative phase microscopies (QPMs) enable label-free, non-invasive observation of living cells in culture, for arbitrarily long periods of time. One of the main benefits of QPMs compared with fluorescence microscopy is the possibility to measure the dry mass of individual cells or organelles. While QPM dry mass measurements on neural cells have been reported this last decade, dry mass measurements on their neurites has been very little addressed. Because neurites are tenuous objects, they are difficult to precisely characterize and segment using most QPMs. In this article, we use cross-grating wavefront microscopy (CGM), a high-resolution wavefront imaging technique, to measure the dry mass of individual neurites of primary neurons in vitro. CGM is based on the simple association of a cross-grating positioned in front of a camera, and can detect wavefront distortions smaller than a hydrogen atom (~ 0.1 nm). In this article, an algorithm for dry-mass measurement of neurites from CGM images is detailed and provided. With objects as small as neurites, we highlight the importance of dealing with the diffraction rings for proper image segmentation and accurate biomass measurements. The high precision of the measurements we obtain using CGM and this semi-manual algorithm enabled us to detect periodic oscillations of neurites never observed before, demonstrating the sufficient degree of accuracy of CGM to capture the

cell dynamics at the single neurite level, with a typical precision of 2%, i.e., 0.08 pg in most cases, down to a few fg for the smallest objects.

<https://pubmed.ncbi.nlm.nih.gov/36589583/>

<https://opg.optica.org/boe/fulltext.cfm?uri=boe-13-12-6550&id=521802>

Sancho-Balsells A, Borràs-Pernas S, Flotta F, Chen W, Del Toro D, Rodríguez MJ, Alberch J, Blivet G, Touchon J, Xifró X, Giralt A. Brain-gut photobiomodulation restores cognitive alterations in chronically stressed mice through the regulation of Sirt1 and neuroinflammation. *J Affect Disord.* 2024 Jun 1;354:574-588. doi: 10.1016/j.jad.2024.03.075.

Abstract

Background: Chronic stress is an important risk factor for the development of major depressive disorder (MDD). Recent studies have shown microbiome dysbiosis as one of the pathogenic mechanisms associated with MDD. Thus, it is important to find novel non-pharmacological therapeutic strategies that can modulate gut microbiota and brain activity. One such strategy is photobiomodulation (PBM), which involves the non-invasive use of light.

Objective/hypothesis: Brain-gut PBM could have a synergistic beneficial effect on the alterations induced by chronic stress.

Methods: We employed the chronic unpredictable mild stress (CUMS) protocol to induce a depressive-like state in mice. Subsequently, we administered brain-gut PBM for 6 min per day over a period of 3 weeks. Following PBM treatment, we examined behavioral, structural, molecular, and cellular alterations induced by CUMS.

Results: We observed that the CUMS protocol induces profound behavioral alterations and an increase of sirtuin1 (Sirt1) levels in the hippocampus. We then combined the stress protocol with PBM and found that tissue-combined PBM was able to rescue cognitive alterations induced by CUMS. This rescue was accompanied by a restoration of hippocampal Sirt1 levels, prevention of spine density loss in the CA1 of the hippocampus, and the modulation of the gut microbiome. PBM was also effective in reducing neuroinflammation and modulating the morphology of Iba1-positive microglia.

Limitations: The molecular mechanisms behind the beneficial effects of tissue-combined PBM are not fully understood.

Conclusions: Our results suggest that non-invasive photobiomodulation of both the brain and the gut microbiome could be beneficial in the context of stress-induced MDD.

Keywords: Declarative memory; Depression; Microbiome; Microglia; hippocampus.

<https://pubmed.ncbi.nlm.nih.gov/38490587/>

<https://www.sciencedirect.com/science/article/pii/S0165032724004907>

Blivet G, Roman FJ, Lelouvier B, Ribi  re C, Touchon J. Photobiomodulation Therapy: A Novel Therapeutic Approach to Alzheimer's Disease Made Possible by the Evidence of a Brain-Gut Interconnection. *J Integr Neurosci*. 2024 Apr 30;23(5):92. doi: 10.31083/j.jin2305092.

Abstract

The evidence of brain-gut interconnections in Alzheimer's disease (AD) opens novel avenues for the treatment of a pathology for which no definitive treatment exists. Gut microbiota and bacterial translocation may produce peripheral inflammation and immune modulation, contributing to brain amyloidosis, neurodegeneration, and cognitive deficits in AD. The gut microbiota can be used as a potential therapeutic target in AD. In particular, photobiomodulation (PBM) can affect the interaction between the microbiota and the immune system, providing a potential explanation for its restorative properties in AD-associated dysbiosis. PBM is a safe, non-invasive, non-ionizing, and non-thermal therapy that uses red or near-infrared light to stimulate the cytochrome c oxidase (CCO, complex IV), the terminal enzyme of the mitochondrial electron transport chain, resulting in adenosine triphosphate synthesis. The association of the direct application of PBM to the head with an abscopal and a systemic treatment through simultaneous application to the abdomen provides an innovative therapeutic approach to AD by targeting various components of this highly complex pathology. As a hypothesis, PBM might have a significant role in the therapeutic options available for the treatment of AD.

Keywords: Alzheimer's disease; brain-gut axis; low-level laser therapy (LLLT); microbiome; microbiota; mitochondria; neurodegeneration; neuroinflammation; oxidative stress; photobiomodulation.

<https://pubmed.ncbi.nlm.nih.gov/38812393/>

<https://www.imrpress.com/journal/JIN/23/5/10.31083/j.jin2305092>

Blivet G, Roman FJ, Delrieu J, Touchon J. Translation from Preclinical Research to Clinical Trials: Brain-Gut Photobiomodulation Therapy for Alzheimer's Disease. *J Integr Neurosci*. 2024 Mar 11;23(3):57. doi: 10.31083/j.jin2303057.

Abstract

Recently, novel non-pharmacological interventions, such as photobiomodulation (PBM) therapy, have shown promise for the treatment of Alzheimer's disease (AD). This article outlines the translation from the preclinical to clinical stages of an innovative brain-gut PBM therapy in a mouse model of AD, a pilot clinical trial involving mild-to-moderate AD

patients, and a continuing pivotal clinical trial with a similar patient population. In a mouse model of AD (A β 25-35), daily application of brain-gut PBM therapy to both the head and the abdomen produced a neuroprotective effect against the neurotoxic effects of an A β 25-35 peptide injection by normalizing all the modified behavioral and biochemical parameters. The pilot clinical trial to evaluate brain-gut PBM therapy demonstrated the tolerability and feasibility of the novel PBM-based treatment for mild-to-moderate AD patients. Compared to the sham patients, the PBM-treated patients had lower Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) comprehension sub-scores, higher forward verbal spans, and lower Trail Making Test (TMT) Part B (TMT-B) execution times, which suggest an improvement in cognitive functions. This pilot study provided important information for the design of a novel pivotal clinical trial, currently in progress, to assess the efficacy of brain-gut PBM therapy in a larger sample of AD patients. This pivotal clinical trial could demonstrate that brain-gut PBM therapy is a safe, well-tolerated, and efficient disease-modifying treatment for mild-to-moderate AD patients and that it has medical and economic benefits.

Keywords: Alzheimer's disease; amyloid; electromagnetic; magnetic; memory; neuro degeneration; neuroinflammation; oxidative stress; phosphorylated tau; photobiomodulation; photonics.

<https://pubmed.ncbi.nlm.nih.gov/38538226/>

<https://www.imrpress.com/journal/JIN/23/3/10.31083/j.jin2303057>

Escarrat V, Reato D, Blivet G, Touchon J, Rougon G, Bos R, Debarbieux F. Dorsoventral photobiomodulation therapy safely reduces inflammation and sensorimotor deficits in a mouse model of multiple sclerosis. *J Neuroinflammation*. 2024 Dec 18;21(1):321. doi: 10.1186/s12974-024-03294-2.

Abstract

Background: Non-invasive photobiomodulation therapy (PBMT), employing specific infrared light wavelengths to stimulate biological tissues, has recently gained attention for its application to treat neurological disorders. Here, we aimed to uncover the cellular targets of PBMT and assess its potential as a therapeutic intervention for multiple sclerosis (MS).

Methods: We applied daily dorsoventral PBMT in an experimental autoimmune encephalomyelitis (EAE) mouse model, which recapitulates key features of MS, and revealed a strong positive impact of PBMT on the sensorimotor deficits. To understand the cellular mechanisms underlying these striking effects, we used state-of-the-art tools and methods ranging from two-photon longitudinal imaging of triple fluorescent reporter mice to histological investigations and patch-clamp electrophysiological recordings.

Results: We found that PBMT induced anti-inflammatory and neuroprotective effects in the dorsal spinal cord. PBMT prevented peripheral immune cell infiltration, glial reactivity, as well as the EAE-induced hyperexcitability of spinal interneurons, both in dorsal and ventral areas, which likely underlies the behavioral effects of the treatment. Thus, aside from confirming the safety of PBMT in healthy mice, our preclinical investigation suggests that PBMT exerts a systemic and beneficial effect on the physiopathology of EAE, primarily resulting in the modulation of the inflammatory processes.

Conclusion: PBMT may therefore represent a new valuable therapeutic option to treat MS symptoms.

Keywords: Experimental autoimmune encephalomyelitis; Inflammation; Neuroprotection; Photobiomodulation therapy.

<https://pubmed.ncbi.nlm.nih.gov/39696356/>

<https://jneuroinflammation.biomedcentral.com/articles/10.1186/s12974-024-03294-2>

Blivet G, Touchon B, Cavadore H, Guillemin S, Pain F, Weiner M, Sabbagh M, Moro C, Touchon J. Brain photobiomodulation: a potential treatment in Alzheimer's and Parkinson's diseases. *J Prev Alzheimers Dis.* 2025 Apr 25:100185. doi: 10.1016/j.tjpad.2025.100185.

Abstract

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are common neurodegenerative diseases, characterized by the progressive loss of synapses and neurons, leading to cognitive and motor decline. Their pathophysiology includes cerebral lesions, oxidative stress, neuroinflammation as well as brain-gut axis microbiota dysbiosis. Preclinical investigations demonstrated that brain photobiomodulation (bPBM) reduces oxidative stress and inflammation, increases cerebral blood flow and enhance neurogenesis and synaptogenesis, which makes bPBM a promising treatment in AD and PD. This review focuses on the clinical application of bPBM in AD and PD. It aims to provide a scientific overview of the current clinical knowledge, review recent clinical studies findings, and describe future directions and upcoming clinical studies. So far, several clinical studies investigated bPBM therapy, at various parameters, both in patients with AD and related dementia, and PD. All demonstrate bPBM safety and bring valuable clinical information regarding efficacy, with particularly promising results in AD. However, their exploratory design and inconsistent quality lead to a low level of evidence, which currently does not support the widespread use of bPBM in clinical practice. Future clinical research should address two gaps: the need for robust double-blinded RCTs vs sham with a higher number of patients and a longer follow-up, and the need for research focusing on dosimetry to determine which bPBM parameters are optimal. The ongoing or

unpublished clinical studies on bPBM should fill in this gap.

Keywords: Alzheimer; Dementia; Parkinson; Photobiomodulation; Treatment.

<https://pubmed.ncbi.nlm.nih.gov/40287365/>

<https://www.sciencedirect.com/science/article/pii/S227458072500130X?via%3DiHub>

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